.....

Exhibit A

Figure 47 is a schematic representation of a rapid temperature cycler with fluorescence detection at the tip of capillary sample tubes, which is generally indicated at 400.

Provided below is a comparison of the different embodiments of the features of the present invention disclosed herein which include fluorescence detection.

	Characteristic	Single Sample Embodiment	Multiple Sample Embodiments	Multiple Sample Embodiments
•	Capacity	Single samples	Multiple samples	Multiple samples
10	Light Source	LED	Xenon Arc	LED
	Detector	Photodiode	PMTs	Photodiode
	Optical Path	Linear	Separate	Epifluorescent
	Emission Bands	1, 2	1, 2	1, 2, 3, continuous
15	Capillary Illumination	Side/Tip	Side	Tip
	Polarization Capable	Yes	No	No

The rapid temperature cycler with fluorescence detection
at the tip of capillary sample tubes represented in Figure 47
is particularly advantageous. The temperature within the
sample chamber is controlled with a 400 W heating cartridge
(available from Reheat, Inc.) and a DC rare earth brush motor
(available from Escap AG., RPM MAX=15,000, estimated time to

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Exhibit A, cont.

failure 10,000 hours) which drives a chamber fan. For heating, the cartridge is proportionally controlled and the fan is run at a low speed (12 V, 0.5 A) to provide temperature homogeneity throughout the sample chamber. For cooling, the heating cartridge is disabled and the fan is run at maximum speed (27 V, 1.4 A). The fan forces air in the central opening and out the exhaust ports. The heating and cooling elements are symmetrical around a central axis, as are up to 24 samples that are placed in a circular carousel that is positioned with a stepper motor. The stepper motor is microstepped (using devices available from New England Affiliated Technologies) to provide over 10,000 steps per revolution of the carousel.

The optical design of the embodiment represented in Figure 47 is based on paraxial epifluorescent illumination of the capillary tip as previously described (see Figure 31). The excitation source is a "super bright" blue light emitting diode (available from LEDtronics). Fluorescence signals are acquired from integrated detector/filter modules (available from Ealing Electrooptics - 0.5 inch interference filters with high performance silicon photodiodes in TO5 packages). The excitation and detection components are mounted directly on

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Exhibit A, cont.

one circuit board with associated electronics. All optics are 0.5 inches in diameter.

The samples are loaded into composite plastic/glass sample containers as shown in Figures 47A-D. A 5  $\mu$ l sample is added to each tube (Figure 47A) and centrifuged at low speed 5 to place the samples at the capillary tips as 1 cm fluid The entrance port of the composite columns (Figure 47B). plastic/glass container is then sealed with a plastic plug (Figure 47C) and placed in the rapid temperature cycler with fluorescence detection at the tip of capillary sample tubes 10 400 (Figure 47D). As can be discerned from Figures 47A-D, the addition of plastic loading and sealing structures to the capillary sample tubes is a great advantage providing efficient use of glass capillary tubes while retaining the desirable thermal characteristics. Samples can be added to 15 the composite plastic/glass sample containers and centrifuged in a 96-well format, but are loaded into the instrument individually. The composite plastic/glass sample containers fit into brass sleeves that align the tip to the optical focal point as represented in Figure 47. This fit is off-axis, 20 allowing precise alignment of each sleeve at the time of fabrication.

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Exhibit A, cont.

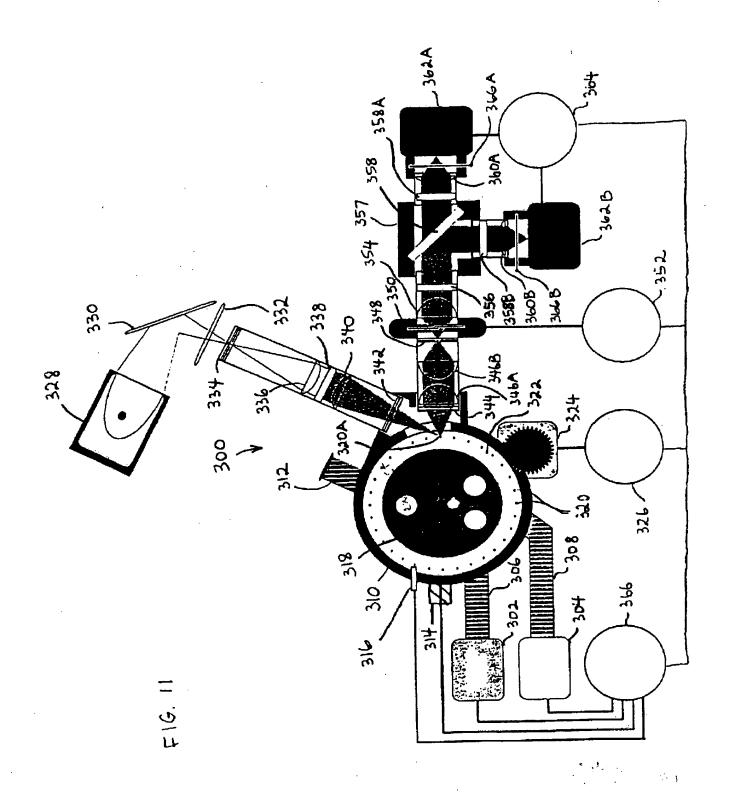


Exhibit A, cont.

